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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|-----------------|-------------|----------------------|---------------------|
|-----------------|-------------|----------------------|---------------------|

08/803, 954 02/21/97 LANGLEY

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HM12/0305

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EXAMINER

HAYES, R.

ART UNIT

PAPER NUMBER

1647

*26*

DATE MAILED:

03/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

**Commissioner of Patents and Trademarks**

|                              |                                      |                                      |
|------------------------------|--------------------------------------|--------------------------------------|
| <b>Office Action Summary</b> | Application No.<br><b>08/803,954</b> | Applicant(s)<br><b>Langley et al</b> |
|                              | Examiner<br><b>Robert C. Hayes</b>   | Group Art Unit<br><b>1647</b>        |

Responsive to communication(s) filed on Apr 20, 2000

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

#### Disposition of Claims

Claim(s) 1-4, 6, 7, 9-11, 31, 32, 37, and 40-43 is/are pending in the application.

Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

Claim(s) \_\_\_\_\_ is/are allowed.

Claim(s) 1-4, 6, 7, 9-11, 31, 32, 37, and 40-43 is/are rejected.

Claim(s) \_\_\_\_\_ is/are objected to.

Claims \_\_\_\_\_ are subject to restriction or election requirement.

#### Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

The proposed drawing correction, filed on \_\_\_\_\_ is  approved  disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All  Some\*  None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_.

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

... SEE OFFICE ACTION ON THE FOLLOWING PAGES ...

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## **DETAILED ACTION**

### ***Continued Prosecution Application***

1. The request filed on 4/20/00 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/803954 is acceptable and a CPA has been established. An action on the CPA follows.
2. The amendment filed 4/20/00 canceling all nonelected claims has been entered.
3. The objection of claims 4, 6-7 & 9-10 should claim 1 be found allowable is withdrawn upon further consideration by the Examiner.
4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
5. Claim 1 stands objected to because reciting sequences by Figure number, versus by the appropriate SEQ ID NO fails to comply with the Sequence rules. Appropriate correction is still required.
6. Applicants are again reminded in that because parent application no. 07/355,027 is at the Board of Appeals, and because the Examiner does not have access to the pending claims on

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appeal, a double patenting rejection may be necessitated if those claims are directed toward metalloprotease inhibitor protein products, as in the instant application.

7. Claims 1-4, 6-7, 9-11, 31-32, 37 & 40-43 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the bovine and human TIMP-2 proteins of Figures 1 & 2, respectively, does not reasonably provide enablement for biologically functional equivalents, or undescribed allelic variants of these TIMP-2-like proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for the reasons made of record in Paper NOs: 19 & 10.

8. Claims 1-4, 6-7, 9-11, 31-32, 37 and 40 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons made of record in Paper NO: 19.

9. Claim 37 stands rejected under 35 U.S.C. 102(b) as being anticipated by Murray et al., for the reasons made of record in Paper NOs: 19 & 10.

10. Claims 1-4, 6-7, 9-11, 31-32, 37 & 40-43 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Stetler-Stevenson et al. (US Patent 5,698,671) (i.e., the straight continuation

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from priority application no. 07/326334 in US Patent 5,595,885), for the reasons made of record in Paper NO: 19.

In summary, Stetler-Stevenson et al. teach isolation and direct partial amino acid sequencing of a native human 23,000 Dalton metalloprotease inhibitor, TCCI (i.e., TIMP-2), which is free of other proteins, either glycosylated or nonglycosylated, and is inherently at least 95% pure with no pyrogen present, as evidenced by the single amino acid sequences obtained, the single band obtained on a 15% polyacrylamide gel under reducing conditions (e.g., col.3, lines 48-52), as well as the disclosure of “purified” in cols.3-4 (i.e., as it relates to claims 1, 3, 31 & 37). Column 2 and Figure 1 indicates that this metalloprotease inhibitor has the biological activity of inhibiting type IV collagenase (i.e., as it relates to claims 1, 10 & 42), and therefore, reasonably also inhibits type 1 collagenase (i.e., as it relates to claim 43); absent evidence to the contrary. In that this protein is immunogenic in generating anti-peptide antibodies (col.4, lines 9-15), the limitations of claims 1, 9 & 41 are met. In that pharmaceutical compositions comprising this protein are disclosed in columns 4 and 6, the limitations of claim 32 are met. In that purified TCCI peptides “can be tagged with suitable enzymatic, fluorescent or radioactive labels” (col. 5), the limitations of claim 32 are also anticipated.

However, the sole differences in sequence between Stetler-Stevenson’s TIMP-2 protein and the 42 amino acid peptide of the instant invention is the conservative substitution of Pro to Asp at position #34, and a conservative substitution back to Pro from an Asn at position #39, in

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which amino acids 40 and 41 were also not sequenced. It is noted that the complete sequence disclosed in Figure 2 is not being claimed in this application.

Thus, because human TIMP-2 is human TIMP-2, because Stetler-Stevenson discloses that “[a]nalog[s] of the natural inhibitor of the invention can be made by preparing peptides and proteins having cysteines at the same intervals as the cysteines in the natural inhibitor (e.g., col.3, lines 8-15), and because these two conservative changes can be considered merely allelic/analog differences between Stetler-Stevenson’s TIMP-2 protein and that currently claimed, these two amino acid substitutions between these two human TIMP-2 peptides are considered a *de minimus* change that would not affect any intrinsic TIMP-2 activity, as evidenced by the metalloproteinase inhibitor function Stetler-Stevenson’s TIMP-2 peptide possesses (e.g., cols. 2 & 4); thereby, not being patentably distinct, and hence obvious, analogous to that held in *Ex parte Anderson*, 30 USPQ2d, 1867 (1994).

It is also noted that the courts have held that when a product (i.e., TIMP-2) in a product-by-process claim (i.e., being synthetic or made recombinantly; col.4, lines 49-62; as it relates to claims 2, 4, 6-7 & 40) is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior art product was made by a different process (*In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983). Further, the courts have held that “when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product..., a

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rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable". *In re Brown*, 173 USPQ 685 (1972).

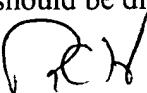
11. All claims are drawn to the same invention claimed in the parent application prior to the filing of this Continued Prosecution Application under 37 CFR 1.53(d) and could have been finally rejected on the grounds and art of record in the next Office action. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing under 37 CFR 1.53(d). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

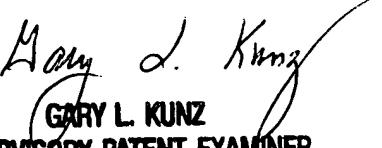
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

  
Robert C. Hayes, Ph.D.  
February 28, 2001

  
GARY L. KUNZ  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600